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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/828,846	04/20/2004	Steven R. Binder	02558B-063710US	5304

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EXAMINER	
WHALEY, PABLO S	

ART UNIT	PAPER NUMBER
1631	

MAIL DATE	DELIVERY MODE
12/31/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/828,846	BINDER ET AL.	
	Examiner	Art Unit	
	PABLO WHALEY	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 August 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *06/05/2009* .
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

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Status of Claims

Claims 1-33 are pending and under consideration. Claim 33 is newly added.

Information Disclosure Statement

The IDS filed 06/05/2009 has been considered in full.

Objections

The objection to claims 1, 18, and 32 is withdrawn in view of applicant's amendments filed 08/19/2009.

Withdrawn Rejections

The rejection of claims 1-17 and 32 are rejected under 35 U.S.C. 101 is withdrawn in view of applicant's amendments filed 08/19/2009, which requires a tie to a computer system and in view of the specification [p.6] which shows the computer system has a processor.

Claim rejections - 35 USC § 112, 1st Paragraph

Claims 33 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection.

This rejection is necessitated by amendment.

Claim 33 (lines 13-14) requires producing a "non-ranked" statistically derived decision. Applicant's response filed 08/19/2009, does not point to support for the newly recited limitations, and no support has been found for this limitation in the specification, drawings, or claims of the application as

originally filed. As the newly recited limitations are not supported by the originally filed claims or disclosure, the claims are rejected for reciting new matter.

Deleted: This rejection is necessitated by amendment.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 6, 10-18, and 22-33 are rejected under 35 U.S.C. 103(a) as being obvious by Zimmerman et al. (Electrophoresis, 1995, Vol. 16, p.941-947), in view of Cabello et al. (Int. J. Biomed. Comput., 1991, Vol. 27, p.77-93), and in view of Kanai (US 5,619,990; Issued: April 15, 1997).

The amended claims are drawn to a computer-implemented method of identifying whether a patient test sample is associated with one or more of a plurality of specific systemic autoimmune diseases (SADs) based on autoantibody levels present in the patient test sample; the method comprising: storing a plurality of reference data sets in a memory, each reference data set having quantitative values representing levels for each of a plurality of specific autoantibodies, wherein said reference data sets include, for each of said plurality of specific SADs, at least one reference data set for the specific SAD, and wherein said reference data sets include at least one reference data set associated with none of the

specific SADs; receiving, in a computer system, a sample data set having quantitative values representing levels for each of said plurality of autoantibodies for a patient test sample; and automatically applying, in the computer system, a k-nearest neighbor process to the quantitative values of the sample data set and the reference data sets to produce a statistically derived decision indicating whether, out of a range of none, one and more than one of said systemic autoimmune diseases, the patient test sample is associated with one or more of said specific SADs, wherein if the decision identifies more than one SAD, the patient test sample is considered equally likely to have said identified SADs; and providing the statistically derived decision as output, the decision identifying which one or more ogthe of said systemic autoimmune diseases the patient test sample is associated with if the statistically derived decision indicates that the patient test sample is associated with one or more of said systemic autoimmune diseases. Newly added claims 33 requires producing a non-ranked statistically derived decision.

Zimmerman teaches a computer-implemented method for identifying whether patient autoantibody samples are associated with autoimmune disease [Abstract]. In particular, Zimmerman teaches obtaining quantitative staining patterns from patients with autoimmune diseases and normal controls [Abstract, Section 2.1], which shows obtaining quantitative sample and reference data wherein at least one data set is associated with none of the diseases. The stained blots are scanned and stored in a database for analysis [Section 2.2, 2.3, 2.4.1, Fig. 3]. Zimmerman shows applying a multivariate discriminate analysis for comparing data of known groups to unknown samples using [p.944, Col. 2, ¶ 2], and providing a statistically derived decision as output [p.945, Col. 2 and Table 1]. Furthermore, their multivariate approach for classifying unknown samples is based on "normal" and "diseased" sample sera, wherein each is described by variables representing a particular staining behavior [p.946, Section 4]. The computer system comprises software and hardware components for implementing the above processes [Section 2.2 and 2.3]. Zimmerman shows the calculation of Chi-squared values (i.e. concordance value) and distance metric values (d') wherein mean known vectors are compared to unknown blot patterns

[p.944, Col. 2, ¶ 3]. Zimmerman shows discarding data if values exceed a certain distance value (i.e. cutoff value) [p.945, Col. 2 and Table 1]. Zimmerman shows increasing said minimal distance and recalculating the analysis [p.945, Col. 2], which is an implicit teaching for a second threshold value. The entire process is implemented on a computer system comprising hardware and software devices [Section 2.2, 2.3].

Zimmerman does not teach applying a k-nearest neighbor process to produce decisions indicating whether, out of a range of none, one or more than one of said systemic autoimmune diseases, the patient test sample is associated with none, one, and more than one of said SADs, wherein if the decision identifies more than one SAD, the patient test sample is considered equally likely to have said identified SADs, as in claims 1, 11-13, 18, 25-28, 32.

Zimmerman does not teach providing a statistically derived decision identifying which one or more of said SADs the patient sample is associated with if the decision indicates that the patient test sample is associated with one or more SADs, as in claims 1, 18, and 32.

Zimmerman does not teach producing a non-ranked statistically derived decision, as in claim 33.

Cabello teaches a k-nearest neighbor algorithm for classifying different types of heart disorders [Abstract]. In particular, the k-nearest neighbor classifiers are assigned to known and unknown data sets [Section 2, p.79-80], and distance calculations are determined [Section 3]. The k-nearest neighbor algorithm is applied to quantitative values of sample data for classification to a plurality of different disease classes [p.83, p.87, Fig. 2]. This method is beneficial for improved data classification [p.78-79].

Kanai teaches an automated method for making statistically derived decisions that identify which specific disease the patient test sample is associated with and if there is no association [Abstract, Fig. 8, 9, 10]. In particular, Kanai teaches a generic discriminant analysis techinque for determining the degree to which a test data group is associated with multiple disease groups or a non-disease control group [Fig. 4, Fig. 7, Col. 6, lines 20-30, Col. 7, lines 30-50, Ref. Claims 20, 28, 30]. The method is based on nearest

neighbor distance between test and reference data [Abstract, Col. 1, Col. 2, Fig. 4, Fig. 7(a)]. This method is beneficial for determining to which of multiple disease groups a patient belongs [Col. 1, lines 5-10].

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention practicing the discriminant analysis method of Zimmerman for identifying patients with SADs to use other known types of discriminant analysis, such as k-nearest neighbor analysis, to produce decisions indicating whether, out of a range of none, one or more than one of said systemic autoimmune diseases, the patient test sample is associated with none, one, and more of said specific SADs, if the decision identifies more than one SAD, the patient test sample is considered equally likely to have said identified SADs, as in claims 1, 11-13, 18, 25-28, 32, since Cabello teaches the classification of one or more different disorders using a k-nearest neighbor algorithm with predictable results [Section 3]. The motivation would have been to employ other known methods of discriminant analysis that provide improved disease classification, as suggested by Cabello [p.79, ¶1]. Zimmerman, Cabello, and Kanai do not specifically teach samples being equally likely to have said identified SADs. However, it would have been obvious to someone of ordinary skill in the art at the time of the instant invention practicing the methods of Zimmerman to identify patient samples that are equally likely to have more than one of the identified SADs since Zimmerman compares probability values for selecting two different SADs wherein at least one pair of them appear to be equal [Fig. 4], since Cabello displays classifier performance and shows at least two different classifiers that identify diseases with the same senstivitiy and specificity [See at least p.89, Table III], and since Kanai shows different types of disease with the same likelihood values [Fig. 8], which reasonably suggests patient samples that are equally likely. The motivation would have been to improve autoimmune disease diagnosis using a discriminant analysis technique that minimizes the possibility for misclassification and allows for the classification of complex data sets, as suggested by Cabello [p.78, last ¶, p.83, p.87, Fig. 2] and Zimmerman [Abstract].

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice the discriminant analysis method of Zimmerman by providing a statistically derived decision identifying which one or more of said SADs the patient sample is associated with if the decision indicates that the patient test sample is associated with one or more SADs, as in claims 1, 18, and 32, since Kanai k-nearest neighbor techniques for making statistically derived decisions that identify which specific disease a patient test sample is associated with, and shows the degre of association and if there is no association, as set forth above, and since Zimmerman shows that discriminant analysis decisions for determining SAD associations are inherently statistically derived [See at least Fig. 4 and Section 4]. The motivation improve disease diagnosis using a method capable of determining if a patient is associated with multiple disease groups, as suggested by Kanai [Col. 1, lines 5-10].

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice the discriminant analysis method of Zimmerman to applying a k-nearest neighbor algorithm to produce a non-ranked statistically derived decision, as in claim 33, since Kanai teaches discriminant process for making statistically derived decisions based on nearest neighbor distances between test and reference data [Abstract, Col. 1, Col. 2, Fig. 4, Fig. 7(a)], and shows predictive values that are of zero value [Fig. 8], which are interpreted as non-ranked decisions. The motivation would have been to improve diagnosis by identifying and elimating groups with no relationship to disease.

Claims 2-5, and 19-22 are rejected under 35 U.S.C. 103(a) as being obvious by Zimmerman et al. (Electrophoresis, 1995, Vol. 16, p.941-947), in view of Cabello et al. (Int. J. Biomed. Comput., 1991, Vol. 27, p.77-93), and in view of Kanai (US 5,619,990; Issued: April 15, 1997), as applied to claims 1, 6, 10-18, and 22-32, above, and further in view of Osterland (CLINICAL CHEMISTRY, 1994, Vol. 40, No. 11(B), p.2146-2153).

Zimmerman, Cabello, and Kanai make obvious a computer-based method for identifying patients associated with none, one, or more autoimmune diseases, as set forth above.

Zimmerman, Cabello, and Kanai do not teach the use of SLE antibody profiles and antigens (Scl-70), as recited in the claims 2-5 and 19-22 and the elected species.

Osterland teaches well known quantitative autoantibody tests and data sets that include antibody concentration and flow cytometry data [Abstract, p.2148, Table 4, Table 5, p.2151, Col. 2, last ¶], including antibodies and antigens comprising SLE, Scl-70, Jo-1 (myositis), and SSA, as recited in the claims 2-4 and 19-22 and the elected species.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the method made obvious by Zimmerman, Cabello, and Kanai by using reference data and sample data having quantitative values representing levels for a plurality of specific autoantibodies, as in claims 1, 18, and 32, since Osterland teaches well known quantitative autoantibody tests and data sets that include antibody concentration and flow cytometry data [Abstract, p.2148, Table 4, Table 5, p.2151, Col. 2, last ¶]. The motivation to use of combination of these antibodies and antigens would have been to provide a more robust test for classifying patients with systemic autoimmune disease [p.2149, Col. 2, p.2152, Col. 1].

Claims 7, 8, and 9 are rejected under 35 U.S.C. 103(a) as being obvious by Zimmerman et al. (Electrophoresis, 1995, Vol. 16, p.941-947), in view of Cabello et al. (Int. J. Biomed. Comput., 1991, Vol. 27, p.77-93), in view of Kanai (US 5,619,990; Issued: April 15, 1997), and in view of Osterland (CLINICAL CHEMISTRY, 1994, Vol. 40, No. 11(B), p.2146-2153), as applied to claims 1-6 and 10-32, and further in view of Kopecky (Design and Implementation of the Internet-Based Medical Expert System ToxoNet, 1999, p.1-153).

Zimmerman, Cabello, Kanai, and Osterland make obvious a computer-based method for identifying patients associated with none, one, or more autoimmune diseases, as set forth above.

Zimmerman, Cabello, Kanai, and Osterland do not teach transmitting display data to a remote computer system, as in claim 7.

Zimmerman, Cabello, Kanai, and Osterland do not teach receiving reference data sets from an automated system over a network connection, as in claims 8 and 9.

Kopecky teaches an internet-based medical expert system (ToxoNet) automated classification of seriological data [p.1]. In particular, Kopecky teaches a server for storing and retrieving data from the database [Section 3.2.2], and transmitting data across a network [Fig. 3.3], and remote computing [Section 3.2.1, and Section 6.2].

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the method made obvious by Zimmerman, Cabello, Kanai, and Osterland by transmitting display data to a remote computer system, as in claim 7, and receiving reference data sets from an automated system over a network connection, as in claims 8 and 9, since Kopecky teaches an internet-based medical expert system (ToxoNet) comprising a server for storing and retrieving data from the database [Section 3.2.2], hardware and software for transmitting data across a network [Fig. 3.3], and remote computing [Section 3.2.1, and Section 6.2]. The motivation would have been to improve disease diagnosis by providing improved communication and remote automated decision support to clinicians.

Response to Arguments

Applicant's arguments filed 08/19/2009 that Zimmerman, Cabello, and Kanai do not teach identifying one or more SADs wherein if the decision identifies more than one SAD, the patient sample is considered equally likely to have more than one of the identified SADs have been fully considered. Broadly interpreted, this claim recites optional language (e.g. if the decision identifies more than one SAD) and a patient sample that is considered equally likely to have the identified SADs. A

review of the specification exemplifies a k-nearest process wherein the distance values of the various points are compared, and when the values for points representing two different diseases differ by less than a minimum difference, both diseases are considered to be equally likely [0030], however these limitations are not recited in the claims. It is acknowledged that Zimmerman, Cabello, and Kanai do not specifically teach samples being equally likely to have said identified SADs. However, it would have been obvious to someone of ordinary skill in the art at the time of the instant invention practicing the methods of Zimmerman, Cabello, and Kanai to identify patient samples that are equally likely to have more than one of the identified SADs since Zimmerman compares probability values for selecting two different SADs wherein at least one pair of them appear to be equal [Fig. 4], since Cabello displays classifier performance and shows at least two different classifiers that identify diseases with the same senstivitiy and specificity [See at least p.89, Table III], and since Kanai shows different types of disease with the same likelihood values [Fig. 8], which reasonably suggests patient samples that are equally likely. The motivation would have been to improve autoimmune disease diagnosis using a discriminant analysis technique that minimizes the possibility for misclassification and allows for the classification of complex data sets, as suggested by Cabello [p.78, last ¶, p.83, p.87, Fig. 2] and Zimmerman [Abstract]. Therefore, the examiner maintains that the combination of references teaches and/or makes obvious the claimed limitations.

Applicant's arguments that Kanai teaches away from the claimed invention because Kanai does not teach an "overlap condition" wherein two diseases are equally likely are not persuasive and cites a passage in Kanai showing the purpose of Kanai is to identify a particular arrythmia. In response, "the prior art's mere disclosure of more than one alternative does not constitute a teaching away from any of these alternatives because such disclosure does not criticize, discredit, or otherwise discourage the solution claimed…." In re Fulton, 391 F.3d 1195, 1201, 73 USPQ2d 1141, 1146 (Fed. Cir. 2004). See also MPEP §2123. Furthermore, Kanai shows different types of disease with the same likelihood values

[Fig. 8], which reasonably suggests patient samples that are equally likely. Therefore, the examiner maintains that the combination of references teaches and/or makes obvious the claimed limitations.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pablo Whaley whose telephone number is (571)272-4425. The examiner can normally be reached between 12pm-8pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached at 571-272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Pablo S. Whaley

Patent Examiner

Art Unit 1631

/PW/

/SHUBO (Joe) ZHOU/

Primary Examiner, Art Unit 1631